#30 JM 7/10/03

Docket No.: **204372000301** (PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of:
Lynn E. SPITLER, M.D., et al

Application No.: 09/300,978 Group Art Unit: 1644

Filed: April 28, 1999 Examiner: P. Gambel

For: PROSTATIC CANCER VACCINE

APPELLANT'S BRIEF

Mail Stop Appeal Brief-Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

Appellants hereby appeal from the final rejection of claims 13, 15, 16, and 18-24 mailed December 30, 2002. A Notice of Appeal was filed along with a Petition for an Extension of Time on April 24, 2003 and was received in the Office on April 29, 2003. As June 29, 2003 is a Sunday, this Brief is believed to be timely filed on the next business day, Monday, June 30, 2003. Appellants respectfully request that the rejection be reversed. In accordance with 37 C.F.R. § 1.192, this Brief is filed in triplicate and is accompanied by the required fee.

sd-150186

I. REAL PARTY IN INTEREST

The present application is assigned to Jenner Technologies, a California Corporation, which was purchased by Immuno-Designed Molecules, a French Corporation.

II. RELATED APPEALS AND INTERFERENCES

Appellants are aware of no interferences and no other appeals which will directly affect or be directly affected by or have a bearing on the Board's decision in this appeal.

III. STATUS OF CLAIMS

A. Total Number of Claims in Application

There are 10 claims pending in application.

B. Current Status of Claims

1. Claims canceled: 1-12, 14, and 16
2. Claims withdrawn from consideration but not canceled: None
3. Claims pending: 13, 15, 16, and 18-24
4. Claims allowed: None
5. Claims rejected: 13, 15, 16, and 18-24

C. Claims On Appeal

The claims on appeal are claims 13, 15, 16, and 18-24.

IV. STATUS OF AMENDMENTS

Applicant filed an Amendment After Final Rejection on February 28, 2003. The Examiner responded to the Amendment After Final Rejection in an Advisory Action mailed March 13, 2003. In the Advisory Action, the Examiner indicated that Appellants' proposed amendments to

claim 13, would be entered. *See* Paper No. 27. Furthermore, the Examiner indicated that the rejections under 35 U.S.C. § 112, first paragraph with regard to written description and enablement for "at least one antigen overrepresented" and "immunologically effective portion" and the rejection under obviousness-type double patenting were overcome in the Amendment under 37 C.F.R. § 1.116 (Paper No. 26). Accordingly, the claims presented in Exhibit A include the amendments proposed in the Amendment submitted under 37 C.F.R. § 1.116 and entered by the Examiner.

V. SUMMARY OF INVENTION

Prior art formulations for vaccines designed to produce an antitumor response from an immune system have been based on the use of antigens that are uniquely associated with the tumors *per se*. The present invention represents a different approach in that, rather than such uniquely tumor-associated antigens as active ingredients, the present invention employs antigens, namely PSMA and PAP, that are associated with the host prostate tissue -- that is, the antigens are found in the prostate in contrast to other tissues. Generally, these antigens are found both in the normal prostate and in malignant prostate tissue. *See* page 4, lines 11-22. The invention takes advantage of the fact that the prostate is not an essential organ and thus an immune response which could include disruption of normal tissue is acceptable. *See* page 4, lines 11-22.

The PAP or PSMA antigen is specifically associated with prostate, whether normal or malignant. The antigen can be supplied, for example, as the antigen *per se* or as an expression system which is able to produce the protein or peptide *in situ* in the subject. The invention is directed to methods of use. *See* paragraph bridging pages 4 and 5.

Thus, the invention of claims 13, 15-16, 18-24 is directed to methods of eliciting an antitumor immune response to prostate tumors using PSMA and/or PAP, or a nucleic acid that generates either antigen as an active ingredient. Claims 20-23 are directed to the same method where either the antigen is further encapsulated in a liposome or coupled to a liposome and/or the liposome contains an adjuvant. The method of claim 24 further defines the method as being directed to a subject afflicted with prostate cancer and/or wherein the subject has been surgically treated to excise the tumor but is at risk for recurrence.

VI. ISSUES

The following issues are presented for review.

1. Whether the instant specification sufficiently describes the "nucleic acid sequences" of the claimed methods to reasonably convey possession of the sequences to the skilled artisan, as reflected in the rejection of claims 13 and 20-24 under 35 U.S.C. § 112, first paragraph.

2. Whether the claimed methods are obvious under 35 U.S.C. § 103 (a) over the combination of Spitler (U.S. Patent 5,783,867) in view of Israeli *et al.* (U.S. Patent 5,538,866), Horoszewicz (U.S. Patent 5,162,504), Andriole *et al.* (*Ann. Rev. Med.* 42: 9-15 (1991)) and in view of the art acknowledged methods of delivering antigens of interest to stimulate antitumor responses and in further evidence of McCarley *et al.* (*Sem. Surg. Oncol.* 5: 293-301 (1989)) alone or in combination with Cruse *et al.* (ILLUSTRATED DICTIONARY OF IMMUNOLOGY (1995)), Kuby (IMMUNOLOGY, 2d ed. (1991)), Paul (FUNDAMENTAL IMMUNOL. 2d ed. (1989)), Grauer (U.S. Patent 5,250,297), Varki (*Cancer Res.* 44: 681-87 (1984)), Linnenbach (U.S. Patent No. 5,185,254) (hereinafter "the '254 patent"), Linnenbach (U.S. Patent No. 5,668,002) (hereinafter "the '002 patent"), and Sela *et al.* (*Hybridoma* 8: 481-91 (1989)).

VII. GROUPING OF CLAIMS

The inventive concept of all claims is the same and all claims may be considered together for purposes of the rejection under 35 U.S.C. § 103. It should be evident that the rejection under 35 U.S.C. § 112, as set forth in Issue 1 above, are inapplicable to claims 15 and 16. Issue 1 relates to whether the specification sufficiently discloses the nucleic acid sequences of the claimed antigens.

VIII. ARGUMENTS

It is believed that issues 1 and 2 should be resolved in favor of appellants for the following reasons:

Issue 1: **Claims 13 and 20-24 are sufficiently described in the instant specification to reasonably convey to the skilled artisan possession of the nucleic acid sequence of the antigens at the time of filing**

A. **Appellants have sufficiently disclosed the nucleic acid sequence of the antigens in the claimed methods to meet the written description requirement of 35 U.S.C. § 112.**

Claims 13 and 20-24 were rejected as lacking sufficient description in the specification to reasonably convey to a person of skill in the art possession of the claimed methods at the time of filing. *See* Paper No. 25, page 2-3. According to the Action, Appellants are required to disclose the nucleic acid sequence itself to satisfy the written description requirement. *Id.*, at page 3. Appellants assert this rejection is in error.

B. **Legal standard of the written description requirement**

In rejecting the presently claimed methods, the Office has apparently taken the position that the nucleic sequence of DNA must be explicitly disclosed in the specification to fulfill patentability requirements of 35 U.S.C. § 112, first paragraph. However, such is not the legal standard for the written description requirement.

The written description requirement prevents an applicant from later asserting that he invented which he did not. *Vas-Cath Inc. v. Mahurkar*, 935 F.2d 1555, 1561, 19 U.S.P.Q.2d 1111, 1115 (Fed. Cir. 1991). In other words, the "description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed." *Lockwood v. Am. Airlines, Inc.*, 107 F.3d 1565, 1572, 41 U.S.P.Q.2d 1961, 1966 (Fed. Cir. 1997). Thus, the test of sufficiency for the requirement is measured by the understanding of one of ordinary skill in the art. *Id.* Therefore, the fulfillment of the written description requirement is a fact-based inquiry that necessarily varies depending on the nature of the invention. *Enzo Biochem v. Gen-Probe, Inc.*, 296 F.3d 1316, 1324, 63 U.S.P.Q.2d 1609, 1613 (Fed. Cir. 2002). Possession of the invention can be shown by actual reduction to practice or showing that the invention was ready for patenting through the description of sufficiently distinguishing characteristics. *See Pfaff v. Wells Electronics, Inc.*, 525 U.S. 55, 68, 48 U.S.P.Q.2d 1641, 1647 (1998).

The written description requirement for genetic material does not require a greater amount of description than other inventions. The amount and type of required description is determined by the understanding of one of ordinary skill in the art. In point of fact, the Federal Circuit has recently addressed the written description requirement for genetic material directly, stating that "*Eli Lilly* did not hold that all functional descriptions of genetic material necessarily fail as a matter of law to meet the written description requirement; rather, the requirement may be satisfied if in the knowledge of the art the disclosed function is sufficiently correlated to a particular, known structure." *Amgen Inc. v. Hoechst Marion Roussel, Inc.* 65 U.S.P.Q.2d 1385, 1398 (Fed. Cir. 2003). Therefore, the sufficiency of a description of genetic material does not necessarily require the disclosure of a nucleic acid sequence, but rather a description sufficient to convey the possession of a known genetic material by the skilled artisan.

C. **The specification sufficiently discloses the known nucleic acid sequence of PAP and PSMA to the skilled artisan.**

Neither PAP or PSMA are unknown or new antigens, and therefore the disclosure in the instant application fulfills the written description requirement under 35 U.S.C. § 112, first paragraph.

First, the antigens and their corresponding nucleotide sequences are known. PAP is disclosed in the specification as a "widely studied antigen" at page 7, lines 21-23. The specification also discloses that the nucleotide sequence of PAP is known and cites two publications that disclose this sequence. *See* specification, page 8, lines 1-5. Similarly, PSMA is disclosed as a known and well-characterized antigen at page 9, lines 9-27 of the instant specification. Appellants also disclose that the nucleotide sequence of PSMA is known and cite a publication that discloses this sequence. *See* specification, page 9, lines 9-11. Therefore, the disclosure in the specification reasonably conveys possession of the antigens of the claimed methods to one of ordinary skill in the art.

Second, the patentability of the instant methods lies not in the invention of PAP, PSMA, or their encoding DNA sequences, but rather in knowing what to do with the antigens. In other words, the patentability lies in the novelty of the method disclosed and not the antigens themselves. Appellants respectfully submit that the Office is improperly applying the written description requirement as if the claimed invention were a novel DNA sequence. While the demonstration of

the conception and reduction to practice of a novel DNA sequence does require the identification of the actual DNA being claimed, it does not follow that the requirement for the recitation of a DNA sequence is applicable to claims involving a method using known proteins and DNA sequences where the patentability lies in the method itself and the sequences are available in the art. As stated above, the Federal Circuit has recently affirmed that all functional descriptions of genetic material do not necessarily fail as a matter of law. *Amgen*, at 1398. Rather the knowledge in the art and the disclosure must be such that one of ordinary skill in the art would comprehend that the applicants had possession of the invention at the time of filing. Appellants submit that the knowledge in the art regarding these proteins and their encoding sequences and the disclosure of this information in the specification is sufficient to convey to the skilled artisan that the Appellants had possession of a particular known DNA sequence for PAP and PSMA at the time of filing. Therefore, the specification fulfills the written description requirement of 35 U.S.C. § 112.

For the reasons stated above, the rejection under 35 U.S.C. § 112, first paragraph may be properly withdrawn.

Issue 2: Claims 13, 15, 16, and 18-24 are nonobvious.

A. The cited references do not render the methods of claims 13, 15, 16, and 18-24 obvious.

Claims 13, 15, 16, and 18-24 were rejected as obvious under 35 U.S.C. § 103 (a) over the combination of Spitler in view of Israeli *et al.*, Horoszewicz, Andriole *et al.* and in view of the art acknowledged methods of delivering antigens of interest to stimulate antitumor responses and in further evidence of McCarley *et al.* alone or in combination with Cruse *et al.*, Kuby, Paul, Grauer, Varki, Linnenbach (the '254 patent), Linnenbach (the '002 patent), and Sela *et al.* Spitler discloses antitumor vaccine compositions and methods useful for the prevention and treatment of a variety of cancers, using tumor antigens that are associated on multiple tumor types. Israeli discloses a form of passive tumor immunotherapy, *i.e.*, therapeutic agents comprising an antibody directed to PSMA that is conjugated to a cytotoxic agent. Horoszewicz relates to passive immunotherapy using prostate-specific antiidiotypic antibodies. Andriole relates to various forms of treatment for prostate

cancer other than immunotherapy. McCarley discloses antibodies against prostate antigens that are useful in passive immunotherapy. Grauer and Varki relate to the generation of antigen-specific antibodies that may be useful in passive immunotherapy. The '254 patent discloses a tumor antigen that is expressed on multiple tumor types, *i.e.*, a pan-epitope. The '002 patent relate to a specific tumor antigen found on multiple tumor types and not on normal tissues. Cruse, Kuby, and Paul relate to the various groupings of tumor antigens. Sela relates to antibodies binding a tumor antigen expressed on multiple gastrointestinal tumors.

The Office has cited a conglomeration of references that do not teach or suggest active immunotherapy using antigens expressed by normal prostate tissue. Therefore, Appellants assert that this rejection is in error.

B. The legal standard of the nonobviousness requirement.

A *prima facie* case of obviousness requires the satisfaction of three requirements. First, the combined references must teach or suggest all of the claim limitations. Second, the references must provide a suggestion or motivation to modify the teachings or combine the references either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. Third, the reference must provide a reasonable expectation of success. *Manual of Patent Examination Procedure* (hereinafter "MPEP") § 2143 (8th ed. 2001).

More specifically, the obviousness analysis under 35 U.S.C. § 103(a) requires the consideration of the scope and content of the prior art, the level of skill in the relevant art, and the differences between the prior art and the claimed subject matter must be considered. *Graham v. John Deere Co.*, 383 U.S. 1, 17 (1966). Critical elements of the invention as a whole which clearly distinguish the entire invention from the prior art references cannot be ignored. *Panduit Corp. v. Dennison Manufacturing Co.*, 1 U.S.P.Q.2d 1593, 1597 (Fed. Cir.), *cert. denied*, 481 U.S. 1052 (1987). Any disclosure teaching away from the claimed invention also must be considered in the obviousness analysis. MPEP § 2142.01. The fact that an invention can be modified is insufficient to establish prima facie obviousness in the absence of a suggestion or motivation to make such a modification. *Id.* Furthermore, if a modification changes the principle of operation of a reference,

the teachings of that reference do not render the claimed invention obvious. *Id.* Finally, in the analysis of prior art references, it is improper to exercise hindsight to select bits and pieces from the references to create a motivation to modify that is not found in the references, but only in the applicant's disclosure. *In re Dow Chemical Co.* 5 U.S.P.Q.2d § 1529, 1531 (Fed. Cir. 1988). Simply stated, the suggestion or motivation to modify a reference must be found in the prior art.

Appellants respectfully submit that a *prima facie* case for obviousness has not been presented. The claimed methods relate to the use of PAP and PSMA, organ-specific antigens, to induce an active antitumor response in a subject. Therefore, a *prima facie* case of obviousness requires that the cited combination of references result in the use of PAP and PSMA to induce an active antitumor response in a subject. The combination of cited references must provide a motivation to combine the teachings of these references to result in the claimed methods, and most importantly, the references must provide a reasonable expectation of success in combining these teachings. For the reasons discussed below, the cited references fail to fulfill these requirements for *prima facie* obviousness.

C. The cited references do not result in the claimed methods.

Appellants respectfully submit that the combination of the cited references does not result in the claimed methods because the references do not teach or suggest the use of PSMA or PAP, organ-specific antigens, in a subject to elicit an active antitumor response. The Examiner seems to rely on the assumption that a demonstration that an antigen can elicit some type of immune response results in the claimed methods using the organ-specific antigens, PAP and PSMA, to elicit an active anti-prostate tumor response. Appellants submit that this point of view is not supported by Spitler, the other cited references, what is known in the art, or any combination thereof.

1. The use of organ-specific antigens is not taught or suggested by the cited references.

All tumor antigens are not alike. Appellants submit that the use of antigens that are organ-specific is a critical element of the claimed methods that cannot be ignored in the obviousness analysis. The elicitation of an immune response to an organ-specific antigen results in the eradication of all antigen-expressing cells whether malignant or normal. Because most organs are

essential for continued viability, such a vaccination strategy is fatal for the recipient unless the targeted organ is non-essential, *e.g.*, the prostate. Thus, vaccination strategy using organ-specific antigens is distinct from vaccination strategies using other types of tumor antigens.

Spitler, the primary reference, fails to teach or suggest the use of organ-specific antigens such as PSMA or PAP to elicit an antitumor response in a subject. PAP and PSMA are organ-specific antigens, expressed solely on normal prostate tissue and prostate tumor tissue, and thus are not uniquely associated with the malignant phenotype of the prostate cells or other tumor cells. In its reliance on Spitler, the Office asserts that antigens uniquely associated with the transformed cell phenotype are equivalent to organ-specific antigens expressed on normal tissue. However, malignancy-associated antigens and organ-specific antigens are not interchangeable in tumor vaccination protocols or otherwise. Spitler teaches the use of antigens that are uniquely associated with the malignant or metastatic nature of the cells. Specifically, Spitler discloses the use of two antigens (*i.e.*, CO-029 and GA733-2) that are each characterized by expression on multiple malignancies. *See* Spitler, at column 2, lines 22-26. Thus, the claimed methods are fundamentally distinct from Spitler in the choice of antigen. The selected antigens are characterized as being expressed on a variety of tumors, not any particular tumor or tissue. In other words, Spitler teaches the use of a pan-epitope to stimulate a general antitumor immune response against any malignant cell. This is distinct from the use of discrete organ-specific antigens used as tumor antigens to elicit an anti-prostate tumor response of the instant claims. Thus, contrary to the assertions of the Examiner, Spitler does not teach the use of organ-specific antigens in vaccine compositions.

None of the references cited by the Examiner rectify this deficiency in Spitler. The CO-029 antigen is not expressed on prostate tumor cells, and therefore neither Sela *et al.* nor the '002 patent teach or suggest the use of PAP and PSMA as in the instant claimed methods. Likewise, the '254 patent does not teach or suggest the use of PAP and PSMA in its disclosure of an antigen expressed in colorectal and pancreatic tumors.

2. Active immunotherapy using organ-specific antigens is not taught or suggested by the combination of cited references.

Appellants respectfully submit that that active and passive immunotherapies are distinct and non-overlapping therapies with distinct antigen requirements and cannot be equated. Because

these therapies are distinct, teachings or suggestions regarding passive immunotherapy does not teach or suggest active immunotherapy. For example, Israeli and Horoszewicz disclose prostate antigens, but neither reference teaches nor suggests the use of an antigen to elicit an active antitumor immune response. Israeli teaches the use of PSMA in passive immunotherapy of tumors. *See* Israeli, at column 12, line 53 to column 13, line 9. Active immunotherapy is not mentioned. Similarly, Horoszewicz teaches the use of prostate antigen-specific antibodies for passive immunotherapy. Horoszewicz's only disclosure of an active immunotherapy protocol does not employ antigen, but uses anti-idiotype antibodies, a fundamentally different therapy (*i.e.*, antigen administration is never required). *See* Horoszewicz, at column 12, lines 21-29. Because Israeli and Horoszewicz do not teach the use of the prostate antigens in active immunotherapy, neither reference alone or in combination with Spitler teach the instant claimed methods.

Andriole *et al.* has no teaching or suggestion regarding the use of prostate antigens to elicit an antitumor response, and thus is not relevant to the claimed methods.

McCarley, Grauer, and Varki have no teaching or suggestion regarding the use of prostate antigens in active immunotherapy. McCarley's teachings are limited the disclosure of a number of monoclonal antibodies that bind various prostate antigens and may be useful for passive immunotherapy (*e.g.*, when conjugated to a chemotherapeutic agent). Grauer and Varki disclose the generation of specific antibodies to non-prostate tumor antigens (*i.e.*, lung carcinoma antigens) without teaching or suggesting the use of these antigen in active immunotherapy of tumors. While Grauer discloses passive immunotherapy, Varki has no discussion of immunotherapy whatsoever. Therefore, as with the references above, if these references are to be relevant to the claimed methods, it must be assumed that the ability to elicit antigen-specific antibodies in non-tumor bearing animals is equivalent to eliciting an effective antitumor response in a subject. Such an assumption cannot be supported scientifically. It is well known in the art the immunogenicity required to elicit specific antibodies that simply bind an antigen does not correlate with, and is often distinct from, the ability to elicit an effective antitumor response, whether humoral or cellular. Thus, these references do not cure the deficiencies in the Spitler reference.

Finally, the Office seeks to use Kuby, Cruse, and Paul to extend Spitler's teachings to the claimed invention. Appellants note that neither Kuby nor Cruse are properly prior art to the claimed invention because the instant priority date is August 11, 1993, and the publication dates for Kuby

and Cruse are 1994 and 1995, respectively. Nonetheless, Cruse lends support to the novelty of Appellants' claimed methods. Cruse classifies tumor-associated antigens into three groups, teaching that "[a]ssays of clinical value will probably be developed for class 2 antigens, since they are associated with multiple neoplasms and very infrequently are found in normal individuals." *See* Cruse, at page 302. In other words, according to Cruse, one of skill in the art would recognize antigens expressed in a variety of tumors with little to no expression in normal tissue as the most likely candidate for active tumor immunotherapy. This definition describes the findings of Spitler, but does not extend them to antigens that are also expressed on normal tissues. Paul does not discuss the relative immunogenicity of the various classes of tumors antigens.

Applicants respectfully submit that the instant claims relate to a method using PAP and PSMA in active immunotherapy, and therefore teachings regarding passive immunotherapy do not render the claims obvious. In other words, the principle of operation in the instant invention is the induction of an immune response in the host through exposure to organ-specific antigens to develop protective immunity, *i.e.*, active immunity. *See, e.g.*, specification at page 4, lines 23-30, and at page 17, lines 11-16. Active immunotherapy requires the administration of an antigen that then induces the host immune system to produce antibodies and/or T cells specific for that antigen that can effectively remove the antigen (and its source). Appellants submit that passive immunotherapy differs in its principle of operation from active immunotherapy. Passive immunity or immunotherapy requires nothing from the host immune system, *i.e.*, the host immune system is passive. The host is the recipient of an agent, typically an antigen-specific antibody derived from another source (*e.g.*, tissue culture, mice, etc.), that mediates its antitumor activity with little or no participation from the host immune system.

In sum, the combination of references cited by the Office do not teach or suggest the use of PAP and PSMA, or antigens with similar characteristics, in active tumor immunotherapy.

D. There is no suggestion or motivation to combine the cited references.

The cited documents provide no suggestion or motivation to combine the teachings to elicit an immune response using antigens expressed in normal prostate tissue. Of all of the references cited by the Office, only Spitler discloses active immunotherapy using antigens of any

type. Because passive and active immunotherapy are functionally and mechanistically distinct, a skilled artisan would have no motivation to combine Spitler with the disclosures teaching passive immunotherapy in Israeli, Horoszewicz, McCarley, Grauer, or Varki.

In fact, Spitler teaches away from the claimed methods. Spitler teaches the need for a vaccine that is "efficacious in the prevention and treatment of all cancers." Spitler, at column 1, lines 50-51 (emphasis added). Spitler also teaches that the disclosed compositions are those useful "for the prevention and treatment of a variety of cancers." Spitler, at column 2, lines 19-21 (emphasis added). In order for such a vaccine to be effective and non-toxic, the target antigen would not be one expressed on normal tissue. A skilled artisan would recognize that the administration of a prophylactic vaccine that elicits an immune response to an antigen on normal tissues would result in autoimmunity specific for that tissue, a potentially fatal side effect. Alternatively stated, Spitler's teachings require the use of antigens that are not expressed on normal tissues to achieve its intended purpose. Hence, nothing in Spitler teaches the extension of its teachings to antigens expressed in an organ-specific manner in normal tissues alone or in any combination with the references cited by the Office.

Because the modification of Spitler's teachings to include organ-specific antigens expressed on normal tissues would render the vaccine unsatisfactory for its intended purpose (*i.e.*, prophylactic and therapeutic vaccine), there is no motivation or suggestion to make such a modification. MPEP § 2143.01 at page 2100-124, second column ("if the proposed modification would render the prior art invention being modified unsatisfactory for its intended purpose, then there is no suggestion or motivation to make the proposed modification") (citations omitted).

Finally, nothing in Spitler, the other cited references, or the art provide a suggestion or motivation to select PAP and PSMA, organ-specific antigens overrepresented in prostate tumors, as antigens for active immunotherapy. It is not true that the use of a pan-epitope for tumor would provide motivation or suggestion to select organ-specific PAP and PSMA as tumor antigens. Spitler's teachings look to a generic tumor epitope, not an organ-specific one. The cited references that merely disclose prostate antigens in unrelated contexts do not provide any suggestion or motivation to use these antigens in Spitler's active immunotherapy of tumors.

E. The combination of references fails to provide a reasonable expectation of success for the claimed methods.

Finally, the references do not provide a reasonable expectation of success in any combination. The majority of the references do not even address active immunotherapy, thus making it impossible for them to convey any expectation of success. Spitler's teaching of active immunotherapy suggests that the use of organ-specific antigens that are also expressed on normal tissues are not candidates for tumor active immunotherapy, thus teaching that such an approach would not be successful.

For the reasons stated above, the rejection under 35 U.S.C. § 103(a) may be properly withdrawn.

IX. CLAIMS INVOLVED IN THE APPEAL

A copy of the claims involved in the present appeal is attached hereto as Appendix A. The claims have been provided based on the format described at 1265 Off. Gaz. Pat. Office 87 (December 17, 2002) and as authorized by Deputy Commissioner for Patents, Stephen Kunin on January 31, 2003. As indicated above, the claims in Appendix A include the amendments filed by Applicant on February 28, 2003.

Dated: June 30, 2003

Respectfully submitted,

By _____

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APPENDIX A

Claims Involved in the Appeal of Application Serial No. 09/300,978

Claims 1-12 (Canceled)

Claim 13 (Previously amended): A method to elicit an antitumor immune response to prostate tumors in a subject, which method comprises

administering to said subject at least one active ingredient formulated for administration to said subject,

wherein said active ingredient comprises or expresses at least one antigen over-represented in the prostate gland,

wherein said antigen is human prostate-specific membrane antigen (PSMA); or

prostatic acid phosphatase (PAP); or mixtures of the foregoing; or

wherein said active ingredient comprises said at least one antigen or a nucleic acid that generates said antigen or antigens *in situ*.

Claim 14 (Canceled)

Claim 15 (Previously amended): The method of claim 13 wherein said active ingredient is human PSMA.

Claim 16 (Previously amended): The method of claim 13 wherein said active ingredient is PAP.

Claim 17 (Canceled)

Claim 18 (Previously amended): The method of claim 13 wherein said active ingredient is a nucleic acid that generates PSMA *in situ*.

Claim 19 (Previously amended): The method of claim 13 wherein said active ingredient is a nucleic acid that generates said PAP *in situ*.

Claim 20 (Original): The method of claim 13 wherein the active ingredient is encapsulated in liposomes and/or coupled to liposomes.

Claim 21 (Original): The method of claim 20 wherein said liposomes contain an adjuvant.

Claim 22 (Original): The method of claim 13 which further includes at least one adjuvant that enhances the antitumor immune response.

Claim 23 (Original): The method of claim 22 wherein said adjuvant is selected from the group consisting of Freund's complete adjuvant; alum; lipid A; monophosphoryl lipid A; *Bacillus Calmette-Guerin* (BCG) or other bacteria polysaccharides; saponins; detoxified endotoxin (DETOX); muramyl tripeptide or muramyl dipeptide or their derivatives; SAF1; lymphokines; cytokines; colony stimulating factors; nonionic block copolymers; and immune stimulating complexes (ISCOMS).

Claim 24 (Original): The method of claim 13 wherein said subject is afflicted with metastatic prostate cancer; and/or wherein said subject has been surgically treated to excise said tumor but is at risk for recurrence.